C. Remarks

The above amendments to claims 28-29 are made to correct the typographical error that resulted in these claims depending from dependent claim 27, instead of independent claim 26.

RESPONSE TO OFFICIAL ACTION OF NOVEMBER 18, 2004

A. Status of the Claims

Claims 1-39 were pending in the case at the time of the Official Action, dated November 18, 2004. All claims stand rejected. Claims 1-39 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of adequate written description. Claims 1-39 also stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Finally, claims 1-39 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over GIBCO BRL Products & Reference Guide (page 20-15, 1997; GIBCO). Applicant offers the following remarks with regard to the above rejections as applied to the presently pending claims.

B. Rejection Based on 35 U.S.C. § 112, First Paragraph, for Failing to Comply With the Written Description Requirement is Overcome

Claims 1-39 stand rejected under 35 U.S.C. § 112, first paragraph, "as failing to comply with the written description requirement." In a Response filed July 29, 2004, Applicant set forth in great detail how the claims satisfy the written description requirement. Applicant believes the continued rejection of the present claims based on failure to comply with the written description requirement is due to a fundamental misunderstanding of the invention. This misunderstanding has led to the argument that the specification does not describe the invention in such a way as to reasonably convey to one skilled in the relevant art that the inventors possessed the claimed invention at the time of filing.

The methods and devices of this invention facilitate the extraction of nucleic acid onto a solid phase directly from a liquid mixture, (*e.g.* a biological or biochemical sample) by drawing

the mixture onto and through the solid phase in one direction, and then forcing it back across the solid phase in the other direction. This novel approach is a quick and easy extraction process in which the "reverse flow" prevents the crude sample from clogging the solid phase, for example by forcing the particulates, debris and viscous material back out of the extraction device. This approach also increases the exposure of nucleic acid in the liquid mixture to the solid phase, because the liquid takes more than one "route" (in more than one direction) through the solid phase. This results in better mixing, which improves nucleic acid binding to the solid phase. Thus, the nucleic acid is extracted from the liquid mixture by immobilizing it on the solid phase.

This is a significant improvement over prior art methods which either passed the nucleic acid sample through the solid phase under gravity (which is an extremely slow process due to the clogging and blockages caused by the particulates, debris and viscous material), or forced the nucleic acid sample through the solid phase in only one direction by applying pressure in an attempt to speed up the process. Both of these methods result in frequent failures, as well as less efficient isolation of nucleic acid from liquid mixtures. Thus, the present invention improves binding of nucleic acid to a solid phase directly from a crude starting material, speeds-up the extraction process, minimizes contamination of the extraction equipment, and facilitates disposal of waste starting material.

The first misunderstanding of the claimed invention set forth in the Action is that "any crude material that was located in the device would be reintroduced to the now eluted nucleic acid." Applicant is puzzled by this assertion, and no scientific support is provided by the Action for this statement. As set forth in the specification, the reverse suction means can force the crude material through the solid phase and out of the extraction device, leaving the nucleic acid bound to the solid phase (and extracted from the liquid mixture). One of skill in the art could certainly

choose to wash the device before eluting the nucleic acid, *e.g.*, as set forth in claim 5, but this step is not essential to the claimed invention. The Action asserts that since the claimed "method does not require the removal or separation of any portion of the liquid sample for the device used to extract nucleic acids therefrom," the "applicant is arguing limitations not found in the claims." But neither removal or separation of the liquid sample is required for the claimed invention, which is directed to *extracting* nucleic acid from a liquid mixture. Once the nucleic acid binds to the solid phase, the nucleic acid is extracted from the liquid sample. While the liquid sample is preferably discarded, *e.g.*, as set forth in claim 4, this is not a necessary step to meet the claimed function of *extracting* nucleic acid from the liquid sample.

Next, the Action argues that the solid phase would be reintroduced into the final preparation of the nucleic acids. Clearly, the specification discloses a variety of means for retaining or directing the placement of the solid phase, and that nucleic acids can be eluted from the solid phase without reintroducing the solid phase into the final preparation. Indeed, Applicant cannot find a disclosure in the specification to support this assertion by the Action, and the Action itself provides no such support. Also, as explained above, the independent claims of the present application do not require that the nucleic acid be eluted from the solid phase. Once again, while the nucleic acid is preferably eluted from the solid phase, *e.g.*, as set forth in claim 6, this is not a necessary step to meet the claimed function of *extracting* nucleic acid from a liquid sample.

The Action next argues that the "specification fails to provide an adequate written description of how any liquid mixture comprising a biological or biochemical mixture is to be extracted from any contaminant with the very method allows [sic] for the retention, if not remixing, of the very contaminants with that which one seeks to extract or otherwise isolate and

elute." Again, this argument is based on a misunderstanding of the invention which as clarified above, involves extracting nucleic acids from a liquid mixture by binding to the solid phase.

The Action's observation that none of the Examples in the specification demonstrate isolation of DNA or RNA "without performance of an extraction step" in no way undermines the claimed invention. Of course DNA or RNA can only be isolated through an extraction step, *i.e.*, the binding of the nucleic acid to the solid phase. This is exactly the function of the claimed invention.

The Action's attempt to recite examples that are not present in the specification as being evidence of lack of written description also fails under the law. First, this argument is directed to the scope of the claims, which is an enablement issue, not a written description issue. Second, under the enablement requirement the mere suggestion of the possible existence of non-operational embodiments within the scope of the claimed invention without facts or evidence is inappropriate. An examiner, in relying on what he asserts to be the general knowledge to negate patentability, must articulate that knowledge and place it of record, and must do so with evidence and support, not subjective beliefs that certain embodiments will not work. Although Applicant presented arguments in the July 29, 2004 Response that the Examiner's hypothetically non-operational embodiments are enabled by the specification (see p. 23), even if non-operational embodiments exist within the scope of the claims, this does not necessarily mean that the claims are unpatentable. *Texas Instruments v. U.S. International Trade Commission*, 231 USPQ 833, 835 (Fed. Cir. 1986). "Even if some of the claimed combinations were inoperative, the claims are not necessarily invalid... [I]f the number of inoperative combinations becomes significant and in effect forces one of ordinary skill in the art to experiment unduly in order to practice the

claimed invention, the claims might indeed be invalid..." *EMI Group North America Inc, v. Cypress Semiconductor Corp.*, 60 USPQ.2d 1423 (Fed. Cir. 2001).

Here, Applicant has presented numerous embodiments demonstrating possession and enablement of the claimed invention. In response the Action presents hypothetical experiments that the Examiner subjectively believes will not work, but has presented no evidence or support for this position. Thus, the Examiner has not established with any appropriate evidence that any inoperable embodiments are within the scope of the claimed invention. In addition, the Examiner has not met his *prima facie* burden to establish a failure by Applicant to fulfill the written description and enablement requirements.

Next, the Action argues that "[w]hile one may assert that it would be obvious for one of skill in the relevant art to modify or adapt the disclosure so to isolate nucleic acids from other sources, obviousness cannot be relied upon for satisfaction of the written description requirement." The Action concludes: "It would appear that applicant is attempting to satisfy the written description requirement... through obviousness." The Action present no evidence for this assertion, and Applicant certainly is not relying on obviousness to satisfy the written description requirement, but rather is relying on Applicant's specification, as previously set forth in great detail. For example, Applicant's use of the terms "biological or biochemical sample" in the claims finds support in the specification (see July 29, 2004 Response, p. 22), and those of skill in the art will understand the identity of the members in this genus (See *Amgen, Inc. v. Hoechst Marion Roussel, Inc.*, 65 USPQ 1385, 1398 (Fed. Cir. 2003) ("the words 'vertebrate' and 'mammalian' readily 'convey[ ] distinguishing information concerning [their] identity' such that one of ordinary skill in the art could 'visualize or recognize the identity of the members of the genus.'" (internal citations omitted)).

In addition, according to the Federal Circuit, Applicant is not required to disclose how to make and use every possible variant of the claimed invention. Instead, Applicant can rely on the disclosure, together with the knowledge of one of skill in the art, to enable the claimed invention:

> That is not to say that the specification itself must necessarily describe how to make and use every possible variant of the claimed invention, for the artisan's knowledge of the prior art and routine experimentation can often fill gaps, interpolate between embodiments, and perhaps even extrapolate beyond the disclosed embodiments, depending upon the predictability of the art. *Chiron Corp. v. Genentech, Inc.*, 363 F.3d 1247, 1253 (Fed. Cir. 2004) (citing *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1244 (Fed. Cir. 2003)).

Finally, the Action maintains a number of specific arguments, such as that the "disclosure fails to locate an adequate written description of pores of some other dimension" other than a range from 1 micron to 150 microns; that the disclosure fails to describe "alternative embodiments of a by-pass channel"; and that the specification "fails to find an adequate written description of how such a device is to be reproducibly made and used." As stated earlier, Applicant clearly demonstrated that there is written description in the specification in response to each of these rejections in the previous Response filed July 29, 2004. For example, page 24 of the Response explains that the specification describes pore sizes of 1-20 microns, 20 microns or larger, 1 to 200 microns, and 0.1mm or greater.

Based on the above arguments, and the failure of the Action to present any arguments or evidence to meet its burden to show that Applicant was not in full possession of the claimed invention as of the filing date, the rejection of claims 1-39 for failing to comply with the written description requirement under 35 U.S.C. § 112, first paragraph, is untenable and should be withdrawn.

C. Rejections Based on 35 U.S.C. § 112, First Paragraph, for Lack of Enablement are Overcome

Claims 1-39 stand rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the enablement requirement. In a Response filed July 29, 2004, Applicant set forth in great detail how the claims satisfy the enablement requirement. In response, the present Action offers the following statement to rebut Applicant's demonstration of enablement: "It is well settled that one cannot enable that which they do not yet possess." But this simply is not true as a matter of law.

As clearly set forth in the Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1, "Written Description" Requirement, 66 Fed. Reg. 1099, 1101 (Jan. 5, 2001): "The enablement and written description requirements are not coextensive and, therefore, situations will arise in which one requirement is met but the other is not... In fact, *Fiers v. Revel* and *Eli Lilly* involved special circumstances where the disclosure of a process of making and the function of the product alone did not provide an adequate written description for product claims." Therefore, the conclusory argument by the Action that because Applicant has not provided written description of the claimed invention, Applicant necessarily has not enabled the invention is incorrect under the law, as reflected in the PTO's Guidelines, and does not meet the Examiner's burden to establish a *prima facie* case of lack of enablement.

This distinction is again set forth by the Federal Circuit in *Univ. of Rochester*, as explained by MPEP § 2163(II.A.3.a): "The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening

compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that '[w]ithout such disclosure, the claimed methods cannot be said to have been described.'" (*citing Univ. of Rochester*, 69 USPQ.2d at 1894-95). Thus, although the claimed invention in *Univ. of Rochester* was arguably enabled because the specification disclosed methods that could be used to identify the claimed compounds, since the patentee did not actually identify any such compounds, the claims were held invalid for lack of written description.

Contrary to the Examiner's assertion, it is not "well settled that one cannot enable that which they do not yet possess." Therefore, the Examiner cannot rely on this conclusory assertion to establish a *prima facie* case of lack of enablement. In addition, as set forth above, one of skill in the art would clearly understand that Applicant possessed the claimed invention at the time the application was filed, in contrast to *Univ. of Rochester*.

Next, the Action argues that Applicant's response setting forth how the claims are enabled by the specification was "conclusory... and has not been found persuasive." Applicant submits that the specification more than adequately teaches one how to make and how to use the claimed subject matter without undue experimentation, as set forth in detail in the Response filed July 29, 2004.

We remind the Examiner that a patent specification need not teach and preferably refrains from teaching that which is well known in the art. To be enabling, the specification must teach those skilled in the art how to make and use the full scope of the claimed invention without "undue experimentation." *In re Vaeck*, 20 USPQ.2d 1348, 1444 (Fed. Cir. 1991). The Action ignores this requirement, and instead argues that even though the "specification may well

disclose various embodiments...," it did not teach enough examples of the claimed invention to satisfy the Examiner. But nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971).

Under MPEP § 2164.04, "In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention." The Examiner has not met this burden to establish a *prima facie* case of lack of enablement because the examiner has not provided a careful consideration of the level of one of ordinary skill in the art, or appropriate evidence to establish that any experimentation required for extracting nucleic acid from a liquid using the claimed invention would be undue. Instead the Examiner has only offered conclusory statements to argue that the claims are not enabled, which is not sufficient to maintain this rejection. Accordingly, Applicant respectfully asserts that the all of the claims are enabled as required under 35 U.S.C. § 112, first paragraph.

D. Rejection Based on 35 U.S.C. § 112, Second Paragraph, for Indefiniteness is Overcome

Claims 28-30 were rejected under 35 U.S.C. § 112, second paragraph, "as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Specifically, the Action states that the claims are unclear because the claims depend from claim 27, which stipulates that "the solid phase is located with the barrel of the syringe," while claims 28-30 have the solid phase in a different part of the syringe.

Applicant has amended claims 28 and 29 so that they depend from independent claim 26, rather than from dependent claim 27, which was clearly a typographical error. Since claim 30 depends from claim 29, it was not amended to change its dependency. These amendments now render claims 28-30 definite. Accordingly, Applicant respectfully requests withdrawal of this rejection.

E. Rejections Based on 35 U.S.C. § 102(b) and 35 U.S.C. § 103(a) are Overcome

Claims 1-39 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over GIBCO BRL Products & Reference Guide (page 20-15, 1997; GIBCO). The Action argues that the columns advertised by GIBCO, and "related methods of using same, are considered to meet the limitation of extracting nucleic acid from a biological or biochemical liquid sample."

Applicant respectfully points out that while the claimed subject matter is directed to extracting nucleic acid from a biological or biochemical liquid sample, the Action ignores the fact that the claimed subject matter also requires a *reversible suction means*. The GIBCO reference clearly does not disclose any columns or devices with a reversible suction means, for example that first draws a liquid mixture through the solid phase of the column or device in one direction and then forces the liquid mixture back over the solid phase in the reverse direction. Nor does this reference in any way suggest that the disclosed columns could be used in such a way. As Applicant has pointed out, prior art methods are disclosed which force liquid mixtures through a solid phase using, for example, a pipette or syringe, *but only in one direction*. Thus, the columns advertised by GIBCO do not anticipate the presently pending claims, nor do they at any point suggest the advantages associated with the reversible suction means. Accordingly,

Applicant respectfully request withdrawal of the rejections under 35 U.S.C. § 102(b) and § 103(a).

CONCLUSION

In light of the foregoing amendments and remarks, Applicant respectfully submits that all claims are in condition for allowance, and solicits an early indication to that effect. Should Examiner Sisson have any questions regarding this response, please contact the undersigned at (512) 542-8569.

Please date stamp and return the enclosed postcard evidencing receipt of these materials.

Respectfully submitted,

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